REMARKS

Claims 1-64 are in this application. Claims 45-62 have been examined. Claims 1-44 have been withdrawn. Claims 42, 45-52, 55-58, and 60-62 have been amended. The amendments will be discussed below.

Claims 63 and 64 have been added. Support for these claims is found in the prior version of claims 50 and 58 and in paragraph [0055] of the specification.

RESTRICTION REQUIREMENT

In the Official Action, the Examiner includes a requirement to restrict the claims of this application to one of eleven groups. The groups identified by the Examiner are set out on pages 3 to 5 of the Action.

Applicant respectfully traverses this restriction requirement.

It is submitted that the claims define a single invention and that all of the claims should be examined in this application. The claims define an invention which is methods of testing for lipid peroxide, pyroglutamic acid and glutathione and comparing the amounts of these compounds before, during and after treatment with an antioxidant. The kit of claims 29-32 may be used for this purpose.

If the Examiner still does not agree that all the claims should be examined in this application, the claims of Group II, namely claims 45-62 are provisionally elected.

All rights to file one or more divisional applications directed to the subject matter of the nonelected claims and/or any other subject matter disclosed in the specification are preserved.

ABSTRACT

The Examiner states in paragraph numbered 12 of the Action that the comma should be deleted after the phrase "needed for" in line 8 of the abstract. Applicant respectfully disagrees. This part of the abstract refers to methods for 1) assessing the need for therapy, 2) utilization efficiency of the therapy and 3) the effectiveness of therapy. Therefore, the use of the comma after the phrase "needed for" is proper.

SPECIFICATION

The words IMMUNE FORMULATION are capitalized in the specification. IMMUNE FORMULATION 100™ is described in paragraph [0054] of the specification and IMMUNE FORMULATION 200™ is described in paragraph [0055] of the specification. Therefore, there is no need to include the generic terminology each time the trademark is used.

Paragraphs [0110], [0112] and [0113] have been amended to capitalize the trademarks BIOXYTECH® and AMSCOT™.

CLAIM OBJECTIONS

Claims 51, 52, and 56-58 have been amended to correct the word anti-oxidant.

Claims 52 and 57 have been amended to insert a comma following word glycine.

Claim 55 has been amended to insert a comma following the word "standard" in lines 14 and 17. Applicant respectfully disagrees with the Examiner

that a comma is needed after the word "subject" in line 5.

Claim 60 has been amended to insert a comma following the word "standard" in lines 3 and 5.

35 USC 112, first paragraph

Claims 51 and 56 have been amended to define the protein as from about 65% to 100% undenatured.

According to the Examiner claims 55 and 60 are rejected under 35 USC 112, first paragraph as failing to comply with the written description requirement. This is respectfully traversed.

The written description and support for these claims is found, *inter alia,* in paragraphs numbered [0012], [0016], [0040], [0041], [0048], [0049], [0069] and [0100] of the specification.

Therefore, it is respectfully requested that these rejections be withdrawn.

35 USC 112, second paragraph

Claim 45 has been amended so the rejections under 35 USC 112, second paragraph set out in numbered paragraphs 23, 24, 25, and 28 as to this claim are moot. In regard to the rejections in numbered paragraphs 26 and 27, the amount of lipid peroxide and pyroglutamic acid in said sample and the level of blood plasma glutathione are being measured. Despite Patent Office practice relating to antecedent basis for a claim element, it is grammatically incorrect to define the amount as "an" amount because it is the amount of lipid peroxide and pyroglutamic acid in the sample that is being measured and it is "the" level of plasma glutathione

that is being measured, not "a" level of plasma glutathione. Therefore, it is respectfully requested that rejections set forth in paragraphs 26 and 27 of the Official Action be withdrawn.

Claim 46 has been amended so the rejections under 35 USC 112, second paragraph set out in numbered paragraphs 29 and 30 as to this claim are moot.

Claim 47 has been amended so the rejection under 35 USC 112, second paragraph set out in numbered paragraph 30 is moot.

The groups of Claims 48 and 49 are Markush groups. As set out in MPEP 2173.05(h), "Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being **"selected from the group consisting of A, B and C."** See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925). Therefore, as Claims 48 and 49 include Markush groups and the terminology "the group" is proper in Markush groups, it is respectfully requested that the rejection set out in numbered paragraphs 31 and 32 be withdrawn.

Claim 50 has been amended to delete the parentheses. Therefore, the rejection under 35 USC 112, second paragraph set out in numbered paragraph 33 is moot.

Claim 50 has been amended to depend from claim 51 Support for this is found in paragraph [0054] of the specification. Claim 58 has been amended to depend from claim 56. As stated above, support for new claims 63 and 64 is found in paragraph [0055] of the specification and in the previous version of claims 50 and 51.

Therefore, the rejection under 35 USC 112, second paragraph set out in numbered paragraph 34 is moot.

Claims 51 and 56 have been amended so the rejection under 35 USC 112, second paragraph set out in numbered paragraph 35 is moot.

It is respectfully requested that the rejection in paragraph 36 be withdrawn. According to the Court of Appeals for the Federal Circuit in Modline Manufacturing Co. v. International Trade Commission , 37 USPQ2d 1609 (Fed. Cir. 1996), the usage of the word "about" can usually be understood in the light of the technology in the invention. Therefore, as one of ordinary skill in the art would understand the meaning of the term "about" in the context of its use in the claims and in view of the specification, it is respectfully requested that the rejection set out in paragraph 36 be withdrawn.

In view of the amendments to claim 55, the rejection under 35 USC 112, second paragraph set out in numbered paragraphs 37-40 are moot.

In regard to the rejections in numbered paragraphs 41 and 42, the amount of lipid peroxide and pyroglutamic acid in the sample and the level of blood plasma glutathione are being measured. It is grammatically incorrect to define the amount as "an" amount because it is the amount of lipid peroxide and pyroglutamic acid in the sample that is being measured and it is "the" level of plasma glutathione that is being measured, not "a" level of plasma glutathione. Therefore, it is respectfully requested that rejections set forth in paragraphs 41 and 42 of the Official Action in regard to claim 55 be withdrawn.

The groups of Claims 61 and 62 are Markush groups. As set out in MPEP

2173.05(h), "Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being **"selected from the group consisting of A, B and C."** See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925). Therefore, as Claims 61 and 62 include Markush groups and the terminology "the group" is proper in Markush groups, it is respectfully requested that the rejection set out in numbered paragraph 43 be withdrawn.

35 USC §103

According to the Official Action, claims 45, 53, 55 and 59 are rejected under 35 USC 103(a) as being unpatentable over Gillam (WO 01/89518) in view of Crawford (US patent 6,709,835) and Ajami (US patent 6,284,219). This is respectfully traversed.

As stated in paragraph [0001] of the specification, "[t]he invention relates to diagnostic methods for assessing the need of a subject for treatment with an anti-oxidant, or alternatively, for determining the effectiveness of anti-oxidant therapy in subjects having been treated with anti-oxidants.

The references cited by the Examiner in combination do not teach a method determining the effectiveness of an anti-oxidant treatment according to claims 45 and 55 and the need for treatment according to claim 55. These methods involve measuring an amount of lipid peroxide and pyroglutamic acid in a sample; measuring the level of blood plasma glutathione; comparing the amount of lipid peroxide and pyroglutamic acid in the sample with that of a normal standard; comparing the level of blood plasma glutathione with that of a normal standard; and

wherein the presence of normal levels of lipid peroxide and pyroglutamic acid in said sample and the presence of normal levels of blood plasma glutathione are an indication of effectiveness of the treatment. Amounts of lipid peroxide and pyroglutamic acid and a level of blood plasma glutathione that is outside of the normal level indicates that need for treatment with an antioxidant.

Section 2141.35 of the Manual of Patent Examining Procedure makes the following points on how an examiner should set about making an assessment of obviousness:

> the following tenets of patent law must be adhered to:
>
> (A) The claimed invention must be considered as a whole;
>
> (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
>
> (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
>
> (D) Reasonable expectation of success is the standard with which obviousness is determined.

In arguing that a claimed invention is obvious, it is, of course, possible to combine teachings from a number of different documents (Orthopedic Equipment Co.v. U.S., 702 F.2d 1005, 217 USPQ 193). In order to do this, however, there needs to be some basis for reading the documents together.

The Federal Circuit summarized its prior case law on the question of the appropriateness of combining prior references to reach a conclusion of obviousness in Ruiz v. A. B. Chance Co., 234 F.3d 654, 57 USPQ2d 1161 (2000).

The reason, suggestion, or motivation to combine may be found

explicitly or implicitly: 1) in the prior art references themselves; 2) in the knowledge of those of ordinary skill in the art that certain references, or disclosures in those references ,are of special interest or importance in the field; or 3) from the nature of the problem to be solved leading inventors to look to references relating to possible solutions to that problem. While the references need not expressly teach that the disclosure contained therein should be combined with another, the showing of combinability must be clear and particular. (Internal citations omitted.)

The Examiner states on page 17 of the Action that according to Gillam, the levels of plasma glutathione progressively decrease from 25 to 45 years of age and that as a consequence the concentration of lipid peroxides rises with age. However, there is no disclosure or suggestion in this reference that there is any treatment that can increase the levels of plasma glutathione or bring it to a normal level or decrease the concentration of lipid peroxides. In addition, as the Examiner states Gillam fails to teach measuring the amount of pyroglutamic acid in a sample.

Crawford does not teach and does not suggest that administering an antioxidant has an effect on the levels of glutathione, lipid peroxides and pyroglutamic acid. Crawford does not teach and does not suggest that measuring the amounts of these compounds can be used to determine the effectiveness and/or the need for therapy with an anti-oxidant. The disclosure that the Examiner refers to at col. 1, lines 64-66 does not teach anything relating to glutathione, lipid peroxides and pyroglutamic acid.

Ajami also does not teach or suggest this. Although in col. 15, lines 54-55 it is stated that the glutathione cycle is responsive to nutritional supplements, this does not suggest treatment with an anti-oxidant or the measurement of glutathione, lipid peroxides and pyroglutamic acid.

There is no combination of the references that teaches or suggests the invention of claims 45, 53, 55 and 59. As stated above,

(A) The claimed invention must be considered as a whole;

(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;

(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(D) Reasonable expectation of success is the standard with which obviousness is determined.

There is no reasonable expectation of success to do what the applicant has done from the combination of references and to suggest otherwise, is relying on impermissible hindsight.

Therefore, it is respectfully requested that the rejection be withdrawn.

According to the Official Action, claims 46-49 and 60-62 are rejected under 35 USC 103(a) as being unpatentable over Gillam (WO 01/89518) in view of Crawford (US patent 6,709,835) and Ajami (US patent 6,284,219) as applied to claims 45 and 55 above, and further in view of Khaled (US Patent 5,977,073). This is respectfully traversed.

For the reasons stated above, the combination of Gillam (WO 01/89518) in view of Crawford (US patent 6,709,835) and Ajami (US patent 6,284,219) do not make obvious claims 45 and 55 and therefore, claims 46-49 and 60-62 cannot be obvious in view of these references even when the Khaled reference is added.

Claim 46 defines that the subject also experienced a reduction in immune cell number, immune function or both, prior to the start of therapy with the anti-oxidant. Claims 47-49 depend directly or indirectly from claim 46. Claim 60 depends from claim 55 and in addition to the measurements of claim 55, defines an additional measurement, "measuring" the number of immune cells. Claims 61-62 depend directly or indirectly from claim 60.

In column 2 of Khaled, a nutritional supplement is disclosed, see for example Table 1. Khaled describes that "the nutritional supplement accelerates replication of the causative virus or bacterium, and creates an ideal condition for the antiorganism agent to exert its maximum effectiveness in killing or injuring the organism." (Col. 2, lines 17-20). However, there is no suggestion in this reference or in the combination of references cited by the Examiner that this nutritional supplement will have any effect on the levels and/or amounts of lipid peroxide, pyroglutamic acid levels and/or blood plasma glutathione.

Therefore, since no combination of the references makes the claimed invention obviousness, it is respectfully requested that the rejection as to claims 46-49 and 60-62 be withdrawn.

According to the Official Action, claims 50, 51, 56 and 58 are rejected under 35 USC 103(a) as being unpatentable over Gillam (WO 01/89518) in view of Crawford (US patent 6,709,835) and Ajami (US patent 6,284,219) as applied to claims 45 and 55 above, and further in view of Crum (WO 99/64022). This is respectfully traversed.

For the reasons stated above, the combination of Gillam (WO 01/89518) in view of Crawford (US patent 6,709,835) and Ajami (US patent 6,284,219) do not make obvious claims 45 and 55 and therefore, claims 50, 51, 56 and 58 cannot be obvious

in view of these references even when the Crum reference is added.

Crum discloses a nutritive composition that are useful in the creation and/or maintenance of a health-protective intestinal bacterial flora and in the enhancement of the immune system. There is no suggestion that this composition or the anti-oxidant compositions of the claimed invention have the effects set out in claims 50, 51, 56 and 58.

Again there is no combination of the references that teach or suggest a method determining the effectiveness of an anti-oxidant treatment according to claims 45 and 55 and the need for treatment according to claim 55. These methods involve measuring an amount of lipid peroxide and pyroglutamic acid in a sample; measuring the level of blood plasma glutathione; comparing the amount of lipid peroxide and pyroglutamic acid in the sample with that of a normal standard; comparing the level of blood plasma glutathione with that of a normal standard; and wherein the presence of normal levels of lipid peroxide and pyroglutamic acid in said sample and the presence of normal levels of blood plasma glutathione are an indication of effectiveness of the treatment. Amounts of lipid peroxide and pyroglutamic acid and a level of blood plasma glutathione that is outside of the normal level indicates that need for treatment with an antioxidant.

Therefore, there is no combination of the references that make the claims 50, 51, 56 and 58 obvious and to state otherwise is to rely on impermissible hindsight.

It is respectfully requested that the rejection be withdrawn.

According to the Official Action, claims 52 and 57 are rejected under 35 USC 103(a) as being unpatentable over Gillam (WO 01/89518) in view of Crawford (US patent 6,709,835) and Ajami (US patent 6,284,219) as applied to claims 45 and 55

above, and further in view of Yegorova (US patent application publication US 2002/0176900). This is respectfully traversed.

For the reasons stated above, the combination of Gillam (WO 01/89518) in view of Crawford (US patent 6,709,835) and Ajami (US patent 6,284,219) do not make obvious claims 45 and 55 and therefore, claims 52 and 57 cannot be obvious in view of these references even when the Yegorova reference is added.

Therefore, it is respectfully requested that the rejection be withdrawn.

The Applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,

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